

## Remarks

The indicated allowability of claim 8 is noted with appreciation. Claim 8 has been rewritten in independent form and presumably is now allowable.

Claims 1-6, 10 and 11 have been rejected as lacking novelty over WO 96/00198. The Examiner also considers claims 1-3, 5-7 and 9-21 to lack novelty over newly cited US 5,922,537 (herein "Ewart").

On review of Ewart, no support can be found for the Examiner's statement that "Ewart et al. teach a phosphorescence biosensor comprising a nanocrystalline metal oxide semiconductor **film upon which** proteins are immobilized" (emphasis added). As understood, Ewart teaches a system where it is the biomolecule which can be immobilized on a substrate, thereby immobilizing the nanoparticle (see, for example, the description of Fig 2, col 4, lines 43-67, where antibodies 40 form a dried film on the plate and nanoparticle reporters 42 are linked to them). It is very widely known that biomolecules can be attached to nanoparticles, and that biomolecules can be attached to surfaces (there are hundreds of papers on both). Furthermore, the introduction of the present application discusses such known processes, see, for example, page 2, lines 11-18. The biosensor of claim 1 and method of claim 17, by contrast, is based upon the use of a film of nanoparticles which are used as the substrate for biomolecule immobilization. This is novel and in the reverse order from Ewart. At no point does Ewart suggest that biomolecules can be immobilized by attachment to a **preformed film of nanoparticles**. Claim 1 has been amended to clarify that the film is preformed to clearly distinguish the claim from the disclosure of Ewart. Such distinction also exists in method claim 17.

Furthermore, the only mention of the composition of the base layer in Ewart appears in claims 6 and 7 which describe a ferroelectric base layer of barium titanate. The patent appears to be focused more on the use of these nanoparticles as sensing elements. There is no suggestion that the nanoparticles are employed or can be construed as being the substrate for biomolecule immobilization. As the Examiner acknowledges, applicants' technology refers to the use of a nanocrystalline film which acts as a base for binding proteins - the film's purpose is the immobilization of these biomolecules and the properties of the sensor are linked to the use of this nanocrystalline substrate. The resulting device, in which the nanoparticles form a rigid, continuous film, is therefore very distinct from that proposed by Ewart et al., both in

terms of film structure and in terms of mechanism of function. Thus, it is respectfully submitted that the claimed subject matter is both novel and not obvious with respect to Ewart.

With regard to the rejection of claims 1-6 and 10-11 as anticipated by WO 96/00198, there still appears to be a misunderstanding. The previously presented comments regarding the use of physiological temperatures is connected with the construction of the device, **not its use**. The Examiner uses the phrase "...the method of intended use of the claimed device (e.g. the claimed physiological temperature) is of no patentable moment...." This could be true if the argument around temperature related to a condition of use of the device. This, however, is not the case: the temperature significant step is during the construction of the device and this impacts on the properties of the device when constructed.

WO 96/00198 uses temperatures of 80°C to immobilize the proteins during manufacture. This means that anybody wishing to construct a device according to the method in WO 96/00198 would not be motivated to use a temperature-sensitive protein that would be denatured if subjected to non-physiological temperatures, inasmuch as such temperatures would then denature the protein. Claim 1 has been amended to make this distinction clear. Support for the amendment can be found at lines 14-16 of page 2 and at lines 6-10 of page 6.

For at least the foregoing reasons, withdrawal of the art rejections is respectfully requested.

In view of the foregoing, request is made for timely issuance of a notice of allowance.

Respectfully submitted,

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